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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,884	05/07/2007	Robin D. Clark	019904-003310US	4264

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EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

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07/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,884	CLARK ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/1/10*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 8-39* is/are pending in the application.

4a) Of the above claim(s) *29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8-28 and 32-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I in the reply filed on 6/1/10 is acknowledged. The traversal is on the ground(s) that the search is not burdensome is not convincing and not persuasive because the structure core changes and is different each structure has a different search and it is burdensome to the PTO. Further the group given by the applicant has been exapanded and includes R1 to be a heteroalkyl along with L1 and l2 to be a bond and an alkylene and R5 is an aryl instead of a phenyl.

The examiner agrees to such an expansion. so group I is now drawn to

to compounds and pharmaceutical compositions of formula II wherein:

- Z^1 is -NR^5-, Z^2 is =N- and Z^3 is =CR^{7a}-, a 1,2,6-triaza-cyclopenta[b]naphthalene core,
- R^1 is a alkylene-N or an alkylene-O group, or a heteroalkyl group,
- R^2 is -X-phenyl or -X-pyridyl,
- L^1 and L^2 are bonds, or alkylene,
- X is a CH_2 or an SO_2, and
- R^5 is an aryl.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement filed 12/11/06 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The copies of the foreign document that was not supplied by the applicant and the examiner could not obtain it also, has been lined through.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3,4,8-28, 32-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for substitutents such as alkyl, halogen, cyano, alkoxy, CF3, alkylcycloalkyl , does not reasonably provide enablement for any and substitutents on the R2 phenyl or pyridine , or and any other substitutent on the R5 aryl and for R7a to be other than H. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds with a tricyclic core and with many substitutents off of the substitutents.

2) The nature of the invention: The invention is a substituted tricyclic azadecalin , gluococorticoid receptor modulator.

3) The state of the prior art: EP 0375210 discloses the compounds with the same core however the substituents are different. These compounds have effects on the central nervous system.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.
5) The level of predictability in the art: Pharmaceutical art is highly unpredictable .

In re Fisher 166 USPQ 18 states:-

It is apparent that such an inventor should be allowed to dominate the future patentable inventions of others where those inventions were based in some way on his teachings. Such improvements, while unobvious from his teachings, are still within his contribution, since the

improvement was made possible by his work. It is equally apparent, however, that he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 U.S.C. 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, ***such as most chemical reactions and physiological activity****, the scope of*

enablement obviously varies inversely with the degree of unpredictability of the factors involved.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification A few examples are made having only limited substitutents, yet the claims have so many substitutents with hetero groups etc. such as

R^{1D} is a member selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, $-NR^{1B1}R^{1B2}$, $-OR^{1B3}$, and $-C(O)NR^{1B4}R^{1B5}$ wherein

R^{1B1} and R^{1B2} are members independently selected from hydrogen, substituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycloalkyl, and substituted or unsubstituted heteroaryl, wherein R^{1B1} and R^{1B2} are optionally joined to form a substituted or unsubstituted ring with the nitrogen to which they are attached, wherein said ring optionally comprises an additional ring heteroatom, and

R^{1B3} is a member selected from hydrogen,substituted or unsubstituted heteroalkyl comprising a nitrogen, substituted or unsubstituted heterocycloalkyl comprising a ring nitrogen, substituted or unsubstituted heteroaryl comprising a ring nitrogen, and alkyl substituted with a substituted or unsubstituted heteroalkyl comprising a nitrogen, substituted or

R^{5A1} is a member selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl, and

R^{5A2} and R^{5A3} are members independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl.

R^{7A1} and R^{7A2} are optionally joined to form a substituted or unsubstituted ring with the nitrogen to which they are attached, wherein said ring optionally comprises an additional ring heteroatom, and

R^{7A3} is a member selected from substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

wherein R^5 is optionally joined with R^{6A} or R^{6C} to form a substituted or unsubstituted ring, wherein said ring optionally comprises an additional ring heteroatom;

wherein R^{7A} is optionally joined with R^{6A} or R^{6C} to form a substituted or unsubstituted ring, wherein said ring optionally comprises an additional ring heteroatom; and

wherein R^{7C} is optionally joined with R^{6A} or R^{6C} to form a substituted or unsubstituted ring, wherein said ring optionally comprises an additional ring heteroatom.

7) The existence of working examples: The instant specification has few compounds made.

The starting materials required for all these substitutents are neither made nor even taught.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome. Also, the eight compounds made do not represent the fullest extent of the instant claim 1.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

The instantly claimed compounds are not structurally similar to known compounds having the same activity and their pharmacological properties can not be predicted from their chemical structure, thus a disclosure that they possess a particular activity is not enough. Thus the specifications fail to provide sufficient support of use of the compounds of the claim for the treatment of all cancers. As a result necessitating one of ordinary skill to perform an exhaustive search for which compounds of the claims can treat all cancers in order to practice the claimed invention.

The specification gives literally no guidance with regard to what the requirements for activity are i.e. which substituents would be preferred. See *Ex parte Herzog, Hershberg, and Coan*, 115 USPQ 195 (Bd. Pat. App. & Int. 1956) affirming the examiner, and stating "it becomes obvious that the expressions defining the organic acids used.....are inclusive of inoperative materials and go far beyond the adequately disclosed subject matter of the specification." And also *Ex parte DIAMOND,* 123 USPQ 167 (Bd. Pat. App. & Int. 1959) where the examiner was affirmed for a scope of enablement rejection, and the court stated:

Scope of claims should not be unduly extensive in chemical fields where applicability is highly speculative or not explored; subject matter which relies upon prediction for its support is unpatentable.
Specification contains 23 specific examples, but they are to preparation of relatively simple compounds; this is relatively meager and non representative disclosure to support claims embracing millions of compounds.
Applicant may not preempt unduly large field by expedient of making broad prophetic statements in specification and claims unless accuracy of such statements is sufficiently supported by well established chemical principles or by sufficient number of examples.
"The term 'substituted' without modification or restriction includes all compounds wherein one or more of the atoms or radicals of the original compound have been replaced by one or more other atoms or radicals. Without any limitation on the character or number of substituents it becomes apparent that the quoted term may be considered inclusive of almost any possible substance and the claims under consideration are either of unlimited or indeterminate scope. We are of the opinion that the reasoning of the courts in Schering Corp. v. Gilbert, 68 USPQ 84, and Hercules Powder Co. v. Rohm & Haas, 70 USPQ 297, is controlling."
embrace millions of compounds. It should also be observed that appellant is working in a field where little prediction is possible and this Board has on several occasions held that the scope of claims should not be unduly extensive in fields where applicability is highly speculative or not explored and that subject matter which relies upon prediction for its support is unpatentable. Ex

parte Middleton, 87 USPQ 57; Ex parte Kauck et al., 95 USPQ 197 , Ex parte Rosenkranz et al., Pat. No. 2,715,637.
In Minnesota Mining and Mfg. Co. et al. v. Carborundum Co. et al., 155 F.2d 746, 69 USPQ 288 , the court held that "An inventor cannot disclose a small number of components which will serve as a springboard for claiming an entire class."

In addition *In re Fouche* 169 USPQ 429 dealt with a similar issue with respect to how to use

requirement of 112 1st paragraph,

"Inclusion of representative examples is not required to enable a person skilled in the art to use a generic invention; nevertheless, applicant must use some technique of providing teaching of how to use which is commensurate with breadth of protection sought by claim, unless such knowledge is already available to persons skilled in the art; thus, where applicant undertakes to define invention by recitation of a Markush group, he must enable one skilled in the art to make and use at least one composition employing each member of group.
Both the examiner and the board noted that none of the working examples pertained to compounds wherein Z was heterocyclic. Appellant is quite correct in contending that, under our decisions in In re Robins, 57 CCPA 1321, 429 F.2d 452, 166 USPQ 552 (1970), the inclusion of representative examples is not required to enable a person skilled in the art to use a generic invention. Nevertheless, an applicant must use *some* technique of providing teaching of how to use which is commensurate with the breadth of protection sought by the claim, unless such knowledge is already available to persons skilled in the art.
It seems clear, and it is not disputed by appellant, that where an applicant undertakes to define his invention by the recitation of a Markush group, he must enable one skilled in the art to make and use at least one composition employing each member of the Markush group. The examiner and the board did not believe that appellant had done so as to the heterocyclic members of the group. While they noted the absence of examples using heterocyclic moieties, we do not find that they viewed examples as mandatory. The issue before us is whether appellant has provided *any* teaching of how to use compounds containing the heterocyclic members of the Markush group. The only reference to heterocyclic radicals in the specification is the statement that "the invention provides" compounds of the structure shown in claim 1, wherein Z may be, among other possibilities, a mononuclear, nitrogen-containing heterocycle connected to the chain A by the nitrogen atom, and optionally containing an oxygen, sulphur, or second nitrogen atom in the ring and optionally substituted by one of more alkyl radicals containing 1 to 5 carbon atoms each, such as 1-pyrrolidyl, piperidino, morpholino, 1-piperazinyl, or 4-alkyl-1-piperazinyl. "

See *Ex parte WEIL AND SCHLICHTING*, 158 USPQ 620 (Bd. Pat. App. & Int. 1967)

"We will sustain this rejection of the claims as we are in accord with the examiner's position. We find no support in the disclosure for such compounds encompassed by these claims wherein R 1, R 2, R 3, and R 5are all the same and selected from the group, lower alkyl ,

hydroxy , alkoxy , di(loweralkyl)amino and nitro for example. These claims appear to be in the nature of a paper concept wherein all possible substituents have been included in the composition. There are no examples of such compounds which are included within the vast scope encompassed by these claims, although appellants have a considerable disclosure with respect to certain components but this does not warrant claims of the enormous breadth recited."

Conclusion

Claims 1,3,4,8-28, 32-39 are rejected.

Claims 29-31 are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

July 14, 2010.